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     (FILE 'HOME' ENTERED AT 11:24:06 ON 26 SEP 2002)

     FILE 'REGISTRY' ENTERED AT 11:24:12 ON 26 SEP 2002
               E ZOLPIDEM/CN
L1             1 S E3

     FILE 'CAPLUS' ENTERED AT 11:25:03 ON 26 SEP 2002
L2           490 S L1
L3             4 S L2 AND HYDRATE

     FILE 'STNGUIDE' ENTERED AT 11:27:25 ON 26 SEP 2002

     FILE 'REGISTRY' ENTERED AT 11:28:43 ON 26 SEP 2002
L4             1 S E4-E5

     FILE 'CAPLUS' ENTERED AT 11:31:15 ON 26 SEP 2002
L5            28 S L4
L6             1 S L5 AND HYDRATE
L7             0 S L6 NOT L3
L8             1 S L5 AND MONOHYDRATE
L9             1 S L8 NOT L3
L10          505 S L2 OR L5
L11            3 S L10 AND POLYMORPH?
L12            3 S L11 NOT L3
L13           27 S L5 NOT L12

     FILE 'MEDLINE' ENTERED AT 11:36:35 ON 26 SEP 2002
L14            0 S L4
L15            1 S ZOLPIDEM (P) HYDRATE

     FILE 'STNGUIDE' ENTERED AT 11:38:42 ON 26 SEP 2002

     FILE 'CAPLUS' ENTERED AT 11:40:56 ON 26 SEP 2002
L16            5 S L10 AND HYDRATE?
L17            1 S L16 NOT L3
L18            0 S L17 NOT L11
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L15 ANSWER 1 OF 1 MEDLINE
AN 2000216611 MEDLINE
DN 20216611 PubMed ID: 10755807
TI Nonselective and selective benzodiazepine receptor agonists--where are we today?.
AU Mitler M M
CS Department of Neuropharmacology, The Scripps Research Institute, La Jolla, CA 92037, USA.. mitler@scripps.edu
SO SLEEP, (2000 Feb 1) 23 Suppl 1 S39-47.
Journal code: 7809084. ISSN: 0161-8105.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200005
ED Entered STN: 20000518
Last Updated on STN: 20000518
Entered Medline: 20000505
AB Insomnia is problematic for many individuals, causing them to seek treatment. There is a long history of therapies aimed at restoring normal sleep patterns, each having its advantages and disadvantages. This review traces the history of insomnia drug therapies from chloral **hydrate** and the barbiturates through the benzodiazepines and explores the newest selective benzodiazepine receptor agonists, including **zolpidem** and zaleplon. The mechanisms of action of the benzodiazepine receptor agonists are compared and contrasted. A pharmacokinetic comparison is presented showing the importance that parameters such as dose, onset of action, lipophilicity, metabolites, half-life, and receptor-binding affinity have on clinical effects. The possible adverse effects of sleep aids are discussed, including residual sedation and psychomotor impairment, daytime anxiety, anterograde amnesia and cognitive impairment, rebound insomnia, and drug tolerance and dependence. Effects on sleep efficiency and staging are also discussed. Recommendations for the primary care physician on the selection of hypnotics are also provided. Benzodiazepine receptor agonists are often appropriate agents in the treatment of insomnia; however, individual drug and patient considerations are important in matching the most appropriate agent to the individual patient. **Zolpidem** and zaleplon, newer selective benzodiazepine receptor agonists, offer additional treatment options.
AB . . . normal sleep patterns, each having its advantages and disadvantages. This review traces the history of insomnia drug therapies from chloral **hydrate** and the barbiturates through the benzodiazepines and explores the newest selective benzodiazepine receptor agonists, including **zolpidem** and zaleplon. The mechanisms of action of the benzodiazepine receptor agonists are compared and contrasted. A pharmacokinetic comparison is presented. . . of insomnia; however, individual drug and patient considerations are important in matching the most appropriate agent to the individual patient. **Zolpidem** and zaleplon, newer selective benzodiazepine receptor agonists, offer additional treatment options.

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=> d 1-3 fbib abs

L12 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS
AN 2001:798053 CAPLUS
DN 135:348889
TI Zolpidem hemitartrate **polymorphs** for treatment of insomnia
IN Aronhime, Judith; Dolitzky, Ben-Zion; Kordova, Marco; Leonov, David; Meszaros-Sos, Erzebet; Salyi, Szaboles; Schwartz, Anchel; Szabo, Csaba; Zavurov, Shlomo
PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001080857	A1	20011101	WO 2001-US13175	20010424
WO 2001080857	C2	20020627		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

			US 2000-199298PP	20000424
			US 2000-206025PP	20000522
			US 2000-225364PP	20000814
US 2002077332	A1	20020620	US 2001-841025	20010424
			US 2000-199298PP	20000424
			US 2000-206025PP	20000522
			US 2000-225364PP	20000814

this appl

AB The present invention provides for novel **polymorphs** of zolpidem hemitartrate and the prepn. of the **polymorphs**. The zolpidem hemitartrate are prepd. as hydrates or solvates, e.g., zolpidem hemitartrate methanolate or acetonate. For example, 5 g (17.7 mmol) of zolpidic acid was suspended in 50 mL of toluene and 0.15 mL of DMF and the mixt. was cooled to 15-28.degree.. Then, 1.7 mL (23.3 mmol) of thionyl chloride was added into the mixt. at this temp. for 1 h, then it is stirred for 4 h at 35-40.degree.. After formation of acid chloride the thionyl chloride excess was removed by distn. The vol. of the reaction mixt. was adjusted to 50 mL by toluene, then it was cooled to -5-0.degree., and dimethylamine gas was introduced into the reaction mixt. until the pH was 8.5-9.5. Pptn. of zolpidem base started almost immediately. The suspension was cooled to -10-(-12).degree. and mixed for 1 h. The crude product was filtered and washed consecutively with toluene, 5% cooled water soln. of NH_4CO_3 and cooled water. The product was dried under vacuum to obtain 4.1 g (yield 80%) zolpidem base used in prepn. of hemitartrate **polymorphs**.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS
AN 2000:528011 CAPLUS
DN 133:344157
TI Evaluation of the genetic component of variability in CYP3A4 activity: A repeated drug administration method
AU Ozdemir, Vural; Kalow, Werner; Tang, Bing-Kou; Paterson, Andrew D.; Walker, Scott E.; Endrenyi, Laszlo; Kashuba, Angela D. M.
CS Departments of Pharmacology and Pharmaceutical Sciences, University of Toronto, Toronto, ON, M5S 1A8, Can.
SO Pharmacogenetics (2000), 10(5), 373-388
CODEN: PHMCEE; ISSN: 0960-314X
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB The CYP3A4 enzyme contributes to the disposition of more than 60 therapeutically important drugs and displays marked person-to-person variability of the catalytic function. However, the extent of genetic contribution to variability in CYP3A4 activity remains elusive. Recently, we showed that a comparison of between- (SDb2) and within-person (SDw2) variances provides an est. of the genetic component of variability in drug disposition. The aim of the present anal. was to assess the genetic control of CYP3A4 activity in vivo. A computerized literature search was

conducted covering 1966 to Sept. 1999 to identify studies reporting repeated administration of CYP3A4 substrates. The genetic contribution (rGC) to disposition of each CYP3A4 substrate was obtained by the formula (SDb2 - SDw2)/SDb2. The rGC values approaching 1.0, point to overwhelming genetic control, whereas those close to zero suggest that environmental factors dominate. A total of 16 studies with 10 different CYP3A4 substrates were identified (n = 161 subjects). The rGC for hepatic CYP3A4 activity as measured by midazolam plasma clearance or the erythromycin breath test was 0.96 (0.92-0.98) (95% CI) and 0.89 (0.65-0.98), resp. (P < 0.05). The point ests. of rGC for composite (hepatic + intestinal) CYP3A4 activity measured after oral administration of cyclosporine, ethinylestradiol, ethylmorphine, nifedipine and nitrendipine, ranged from 0.66-0.98 (median: 0.83) (P < 0.05). Cyclosporine data suggested a higher genetic control of CYP3A4 at night than during the day. These data indicate that further mol. genetic investigations are warranted to identify genetic variants at CYP3A4 or elsewhere in the genome which contribute to regulation of CYP3A4 activity.

RE.CNT 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS
AN 1999:310588 CAPLUS
DN 131:96890
TI Pharmacologic and behavioral responses of inbred C57BL/6J and Strain 129/SvJ mouse lines
AU Homanics, Gregg E.; Quinlan, Joseph J.; Firestone, Leonard L.
CS Departments of Anestheshiology/Critical Care Medicine and Pharmacology, University of Pittsburgh, Pittsburgh, PA, 15261, USA
SO Pharmacology, Biochemistry and Behavior (1999), 63(1), 21-26
CODEN: PBBHAU; ISSN: 0091-3057
PB Elsevier Science Inc.
DT Journal
LA English
AB Gene-targeting technol. is creating an explosion in the no. of animals available with single gene mutations that affect the function of the central nervous system. Most gene-targeted mice are produced on a mixed genetic background of C57BL/6J and substrains of Strain 129. Understanding the behavioral characteristics and responses to various drugs of these parental strains is vital to interpreting data from gene-targeted mice. We directly compared C57BL/6J and Strain 129/SvJ mouse lines on several behavioral paradigms and in response to several hypnotic and anesthetic drugs. Compared to Strain 129/SvJ mice, C57BL/6J animals are more sensitive to the hypnotic effects of midazolam, zolpidem, and propofol, less sensitive to etomidate and ethanol, and do not differ in sensitivity to Ro15-4513 or pentobarbital. These strains do not differ in their sensitivity to the motor ataxic effects of the volatile anesthetics enflurane or halothane. However, Strain 129/SvJs are more sensitive to the immobilizing effects of halothane but not enflurane. Motor coordination differs initially, but with repeated testing strain differences are no longer apparent. Strain 129/SvJ mice are more anxious on the elevated plus maze and open-field activity assays. Thus, these mouse strains harbor **polymorphisms** that influence some, but not all, traits of interest to behavioral neuroscientists.

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 11:24:06 ON 26 SEP 2002)

FILE 'REGISTRY' ENTERED AT 11:24:12 ON 26 SEP 2002
E ZOLPIDEM/CN
L1 1 S E3

FILE 'CAPLUS' ENTERED AT 11:25:03 ON 26 SEP 2002
L2 490 S L1
L3 4 S L2 AND HYDRATE

FILE 'STNGUIDE' ENTERED AT 11:27:25 ON 26 SEP 2002

FILE 'REGISTRY' ENTERED AT 11:28:43 ON 26 SEP 2002
L4 1 S E4-E5

FILE 'CAPLUS' ENTERED AT 11:31:15 ON 26 SEP 2002
L5 28 S L4
L6 1 S L5 AND HYDRATE
L7 0 S L6 NOT L3

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L8            1 S L5 AND MONOHYDRATE
L9            1 S L8 NOT L3
L10         505 S L2 OR L5
L11           3 S L10 AND POLYMORPH?
L12           3 S L11 NOT L3

=> s l5 not l12
L13          27 L5 NOT L12

=> d 1-3 bib abs

L13  ANSWER 1 OF 27  CAPLUS  COPYRIGHT 2002 ACS
AN   2002:408517  CAPLUS
DN   137:741
TI   Inhibitors of ABC drug transporters at the blood-brain barrier for
     increasing brain concns. of central nervous system-active agents
IN   Schoenhard, Grant L.
PA   Pain Therapeutics, Inc., USA
SO   PCT Int. Appl., 143 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 13
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
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PI   WO 2002041884     A2    20020530       WO 2001-US45367  20011030
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,
             UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 6011004        A     20000104       US 1996-768221   19961217
     AU 9947399        A1    19991028       AU 1999-47399    19990906
     AU 2002039427     A5    20020603       AU 2002-39427    20011030
PRAI US 2000-244482P   P     20001030
     US 2000-245110P   P     20001101
     US 2000-246235P   P     20001102
     US 1990-612847    B1    19901113
     US 1993-153796    A1    19931117
     AU 1995-32769     A3    19950718
     WO 2001-US45367   W     20011030
OS   MARPAT 137:741
AB   The invention relates to inhibitors of drug transporters of the ABC
     protein superfamily, particularly transporters present at the blood brain
     barrier.  ABC transporter inhibitors identified according to the invention
     increase brain concns. of CNS-active agents.  Such inhibitors increase the
     influx into the brain and/or reduce the efflux from the brain of such
     CNS-active agents.

L13  ANSWER 2 OF 27  CAPLUS  COPYRIGHT 2002 ACS
AN   2002:47557  CAPLUS
DN   136:102382
TI   A process for the preparation of 2-phenyl-imidazo[1,2-a]pyridine-3-
     acetamides
IN   Castaldi, Graziano
PA   Dinamite Dipharma S.P.A. (In Abbreviated Form Dipharma S.P.A.), Italy
SO   Eur. Pat. Appl., 18 pp.
     CODEN: EPXXDW
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
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PI   EP 1172364        A1    20020116       EP 2001-116016   20010702
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     US 2002019528     A1    20020214       US 2001-902616   20010712
     US 6384226        B2    20020507
     JP 2002167385     A2    20020611       JP 2001-212175   20010712
PRAI IT 2000-MI1591    A     20000714
OS   CASREACT 136:102382; MARPAT 136:102382
GI
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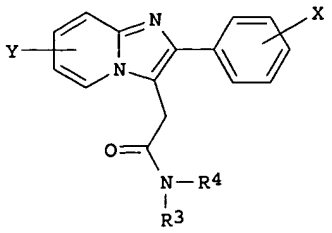

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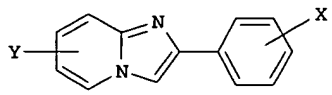

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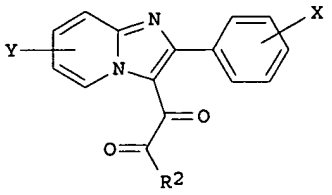

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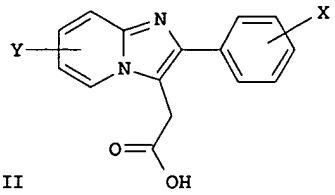

IV

AB A process for the prepn. of 2-phenyl-imidazo[1,2-a]pyridine-3-acetamides (I; X = H, halo, C1-4 alkyl, C1-6 alkoxy, CF3, MeS, NO2, MeSO2; Y = H, halo, C1-4 alkyl; R3, R4 = H, C1-5 alkyl, allyl, propargyl, C3-6 cycloalkyl, CH2Ph, Ph) comprises the reaction of a 2-phenyl-imidazo[1,2-a]pyridine (II; X, Y = same as above) with an oxalic ester reactive deriv. of formula R1COCOR2 (R1 = halo, a carboxy-activating group; R2 = C1-6 alkoxy or phenoxy both optionally substituted with C1-6 alkyl or alkoxy, C1-6 alkylamino, arylamino), followed by reducing the carbonyl group of the resulting glyoxalate esters (III; R2 = = same as above) and reacting the resulting carboxylic acids (IV; X, Y = same as above) with an amine of formula NHR3R4. This process provides an efficient, convenient route for the prepn. of 2-phenylimidazo[1,2-a]pyridine-3-acetamides, in particular zolpidem. All known synthesis of zolpidem used either reagents com. available with difficulty, toxic reagents, or industrially unsuitable procedures due to low yields and/or products with poor purity which should undergo repeated purifn. procedures. Under the best operative conditions, this method gives zolpidem of suitable quality and in yields above 80%, starting from imidazopyridine. Thus, chlorination of potassium monoethyl oxalate with POCl3 in CH2Cl2 at .apprx.30.degree. for 4-6 h followed by acylation of 2-(4-methylphenyl)-6-methylimidazo[1,2-a]pyridine with the resulting oxalic acid chloride Et ester in the presence of Et3N under reflux for 1 h gave 97.5% Et 2-(4-methylphenyl)-6-methylimidazo[1,2-a]pyridine-3-glyoxalate (V). Sapon. of V with NaOH in aq. EtOH under reflux, followed by condensation with hydrazine under reflux for 14 h and distn. in the presence of KOH at 122-14.degree. under refluxing until N evolution ceased gave, after acidification with AcOH, 96.5% 2-(4-methylphenyl)-6-methylimidazo[1,2-a]pyridine-3-acetic acid (VI). Chlorination of VI with oxalyl chloride in CH2Cl2 under reflux for 30 min and amidation with dimethylamine hydrochloride at room temp. for 1 h gave zolpidem which was converted into zolpidem oxalate.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 27 CAPLUS COPYRIGHT 2002 ACS
AN 2001:780683 CAPLUS
DN 135:335156
TI Modified-release formulations containing a hypnotic agent
IN Platteeuw, Johannes Jan; Van Den Heuvel, Dennie Johan Marijn; Van Dalen, Frans; Lemmens, Jacques Maria
PA Synthon B.V., Neth.
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001078725	A2	20011025	WO 2001-NL299	20010412
WO 2001078725	A3	20011220		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 2000-196939P P 20000413

AB Hypnotic pharmaceutical compns. are made from pellets and exhibit a modified release. Zolpidem or a pharmaceutically acceptable salt thereof is a typical hypnotic. The pellets are preferably spherical and exhibit a dissoln. profile that includes 60% of the hypnotic agent being released from the pellet not earlier than 5 min from the start of a specified in vitro dissoln. test. Although the modified release profile can include 50 of the hypnotic agent being released not earlier than 15 min after the start of the dissoln. test, the pellet preferably does not contain a release rate controlling excipient or coating. Instead, microcryst. cellulose and the active constitute the majority of the pellet, e.g. 90 or more. Spherical pellets are also made by a convenient method that is applicable to any pharmaceutically active agent. Microcryst. cellulose 1703, zolpidem hydrochloride hydrate 189.2 g, and water 1892 mL were mixed and stirred for 15 min. Water was then removed and the resulted pellets were dried and fractionated by sieving.

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L9 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
AN 2000:686287 CAPLUS
DN 133:252434
TI Imidazopyridine derivatives and process for making them
IN Ettema, Gerrit Jan Bouke; Lemmens, Jacobus Maria; Peters, Theodorus Hendricus Antonius; Picha, Frantisek
PA Synthon B.V., Neth.
SO Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1038875	A2	20000927	EP 1999-203478	19991022
	EP 1038875	A3	20010912		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 6281360	B1	20010828	US 2000-512789	20000225
	NL 1014634	C1	20000803	NL 2000-1014634	20000313
	WO 2000058310	A1	20001005	WO 2000-NL171	20000313
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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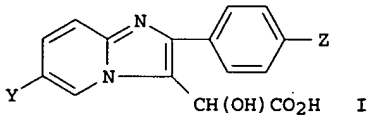
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	US 1999-126494P	P	19990325		
	EP 1999-203478	A	19991022		
	US 1999-449974	A	19991126		
	WO 2000-NL171	W	20000313		

OS CASREACT 133:252434; MARPAT 133:252434
GI



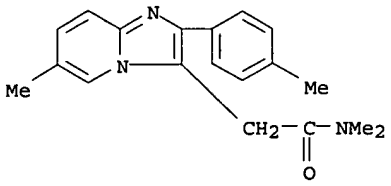
I

AB Imidazopyridines I (Y, Z = lower alkyl) were prepd. by reaction of 6-alkyl-2-(p-alkylphenyl)imidazo[1,2-a]pyridines with glyoxylic acid or its acetal. Thus, 22 g of 6-methyl-2-p-tolylimidazo[1,2-a]pyridine was suspended in 100 mL of dichloroethene, 10 g of glyoxylic acid **monohydrate** was added, and the mixt. was heated to reflux for 1.5 h to give 28 g of I (Y = Z = Me) with a purity of 97.9%.
AB Imidazopyridines I (Y, Z = lower alkyl) were prepd. by reaction of 6-alkyl-2-(p-alkylphenyl)imidazo[1,2-a]pyridines with glyoxylic acid or its acetal. Thus, 22 g of 6-methyl-2-p-tolylimidazo[1,2-a]pyridine was suspended in 100 mL of dichloroethene, 10 g of glyoxylic acid **monohydrate** was added, and the mixt. was heated to reflux for 1.5 h to give 28 g of I (Y = Z = Me) with a purity of 97.9%.
IT 82626-48-0P, Zolpidem **99294-93-6P**, Zolpidem hemitartrate
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

09841025

=> d l1

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 82626-48-0 REGISTRY
CN Imidazo[1,2-a]pyridine-3-acetamide, N,N,6-trimethyl-2-(4-methylphenyl)-
(9CI) (CA INDEX NAME)
OTHER NAMES:
CN SL 80-0750
CN **Zolpidem**
FS 3D CONCORD
MF C19 H21 N3 O
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST,
CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES,
EMBASE, IPA, MEDLINE, MRCK*, NIOSHTIC, PHAR, PROMT, RTECS*, SYNTHLINE,
TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

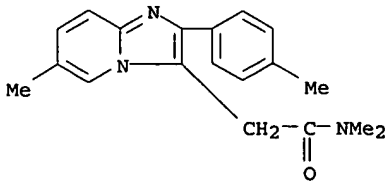
489 REFERENCES IN FILE CA (1962 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
491 REFERENCES IN FILE CAPLUS (1962 TO DATE)

=> s e4-e5
1 "ZOLPIDEM HEMITARTRATE"/CN
1 "ZOLPIDEM TARTRATE"/CN
L4 1 ("ZOLPIDEM HEMITARTRATE"/CN OR "ZOLPIDEM TARTRATE"/CN)

=> d scan

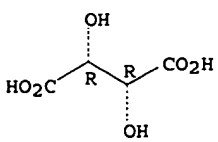
L4 1 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Imidazo[1,2-a]pyridine-3-acetamide, N,N,6-trimethyl-2-(4-methylphenyl)-,
(2R,3R)-2,3-dihydroxybutanedioate (2:1) (9CI)
MF C19 H21 N3 O . 1/2 C4 H6 O6

CM 1



CM 2

Absolute stereochemistry.



09841025

09841025

=> d 1-4 bib abs kwic

L3 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 2001:780683 CAPLUS
DN 135:335156
TI Modified-release formulations containing a hypnotic agent
IN Platteeuw, Johannes Jan; Van Den Heuvel, Dennie Johan Marijn; Van Dalen, Frans; Lemmens, Jacques Maria
PA Synthon B.V., Neth.
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001078725	A2	20011025	WO 2001-NL299	20010412
WO 2001078725	A3	20011220		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-196939P P 20000413

AB Hypnotic pharmaceutical compns. are made from pellets and exhibit a modified release. Zolpidem or a pharmaceutically acceptable salt thereof is a typical hypnotic. The pellets are preferably spherical and exhibit a dissoln. profile that includes 60% of the hypnotic agent being released from the pellet not earlier than 5 min from the start of a specified in vitro dissoln. test. Although the modified release profile can include 50 of the hypnotic agent being released not earlier than 15 min after the start of the dissoln. test, the pellet preferably does not contain a release rate controlling excipient or coating. Instead, microcryst. cellulose and the active constitute the majority of the pellet, e.g. 90 or more. Spherical pellets are also made by a convenient method that is applicable to any pharmaceutically active agent. Microcryst. cellulose 1703, zolpidem hydrochloride **hydrate** 189.2 g, and water 1892 mL were mixed and stirred for 15 min. Water was then removed and the resulted pellets were dried and fractionated by sieving.

AB Hypnotic pharmaceutical compns. are made from pellets and exhibit a modified release. Zolpidem or a pharmaceutically acceptable salt thereof is a typical hypnotic. The pellets are preferably spherical and exhibit a dissoln. profile that includes 60% of the hypnotic agent being released from the pellet not earlier than 5 min from the start of a specified in vitro dissoln. test. Although the modified release profile can include 50 of the hypnotic agent being released not earlier than 15 min after the start of the dissoln. test, the pellet preferably does not contain a release rate controlling excipient or coating. Instead, microcryst. cellulose and the active constitute the majority of the pellet, e.g. 90 or more. Spherical pellets are also made by a convenient method that is applicable to any pharmaceutically active agent. Microcryst. cellulose 1703, zolpidem hydrochloride **hydrate** 189.2 g, and water 1892 mL were mixed and stirred for 15 min. Water was then removed and the resulted pellets were dried and fractionated by sieving.

IT 50-35-1, Thalidomide 2809-21-4 4291-63-8, Cladribine 5630-53-5, Tibolone 5633-20-5, Oxybutynin 9004-34-6, Cellulose, biological studies 12794-10-4D, Benzodiazepine, derivs. 24584-09-6, Dexrazoxane 42399-41-7, Diltiazem 43200-80-2, Zopiclone 51803-78-2, Nimesulide 54024-22-5, Desogestrel 56180-94-0, Acarbose 59729-33-8, Citalopram 61869-08-7, Paroxetine 68291-97-4, Zonisamide 68693-11-8, Modafinil 71620-89-8, Reboxetine 72956-09-3, Carvedilol 75330-75-5, Lovastatin 75706-12-6, Leflunomide 75887-54-6, Artemotil 76963-41-2, Nizatidine 79902-63-9, Simvastatin 80125-14-0, Remoxipride **82626-48-0**, Zolpidem 85650-52-8, Mirtazapine 88150-42-9, Amlodipine 91374-21-9 93413-69-5, Venlafaxine 96829-58-2, Orlistat 99294-93-6, Zolpidem tartrate 103188-50-7 104632-26-0, Pramipexole 105816-04-4, Nateglinide 106133-20-4, Tamsulosin 106266-06-2, Risperidone 107868-30-4, Exemestane 111025-46-8, Pioglitazone 111974-69-7, Quetiapine 112809-51-5, Letrozole 113665-84-2, Clopidogrel 113806-05-6, Olopatadine 115256-11-6, Dofetilide 120014-06-4, Donepezil 122320-73-4, Rosiglitazone 124937-51-5, Tolterodine 130209-82-4, Latanoprost 132539-06-1, Olanzapine 133040-01-4, Eprosartan 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 139481-59-7, Candesartan 144034-80-0, Rizatriptan 144701-48-4,

Telmisartan 146939-27-7, Ziprasidone 151319-34-5, Zaleplon 185243-69-0, Etanercept 299397-15-2 299397-16-3 299397-18-5 299397-19-6 299397-20-9 299397-23-2 299397-24-3 299397-25-4 369371-24-4
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modified-release formulations contg. hypnotic agent)

L3 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 2001:338762 CAPLUS
DN 134:362292
TI Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
IN Farr, Spencer
PA Phase-1 Molecular Toxicology, USA
SO PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001032928	A2	20010510	WO 2000-US30474	20001103
WO 2001032928	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-165398P P 19991105
US 2000-196571P P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to det. the hypersensitivity of individuals to a given agent, such as drug or other chem., in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes assocd. with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes assocd. with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes assocd. with hypersensitivity. The expression of the genes predetd. to be assocd. with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and app. useful for identifying hypersensitivity in a subject are also disclosed.

IT 50-02-2, Dexamethasone 50-06-6, Phenobarbital, biological studies 50-18-0, Cyclophosphamide 50-23-7, Hydrocortisone 50-24-8, Prednisolone 50-28-2, Estradiol, biological studies 50-44-2, 6-Thiopurine 50-48-6, Amitriptyline 50-55-5, Reserpine 50-76-0, Actinomycin D 50-78-2, Aspirin 51-06-9, Procainamide 51-21-8, Fluorouracil 51-34-3, Scopolamine 51-48-9, Levothyroxine, biological studies 51-49-0, Dextrothyroxine 51-55-8, Atropine, biological studies 51-75-2, Mechlorethamine 52-01-7, Spironolactone 52-53-9, Verapamil 52-67-5, Penicillamine 52-86-8, Haloperidol 53-03-2, Prednisone 53-06-5, Cortisone 53-19-0, Mitotane 53-33-8, Paramethasone 53-86-1, Indomethacin 54-05-7, Chloroquine 54-11-5, Nicotine 54-31-9, Furosemide 54-36-4, Metyrapone 54-85-3, Isoniazid 55-63-0, Nitroglycerin 55-65-2, Guanethidine 55-98-1, Busulfan 56-54-2, Quinidine 56-75-7, Chloramphenicol 57-22-7, Vincristine 57-41-0, Phenytoin 57-53-4, Meprobamate 57-63-6, Ethinyl estradiol 57-66-9, Probenecid 57-83-0, Progestin, biological studies 57-96-5, Sulfinpyrazone 58-05-9, Leucovorin 58-14-0, Pyrimethamine 58-32-2, Dipyridamole 58-39-9, Perphenazine 58-54-8, Ethacrynic acid 58-55-9, Theophylline, biological studies 58-61-7, Adenosine, biological studies 58-74-2, Papaverine 58-93-5, Hydrochlorothiazide 58-94-6, Thiazide 59-05-2, Methotrexate 59-42-7, Phenylephrine 59-43-8, Thiamine, biological studies 59-92-7, Levodopa, biological studies 59-99-4, Neostigmine 60-40-2, Mecamylamine 60-54-8, Tetracycline 60-79-7, Ergonovine 60-87-7, Promethazine 61-32-5, Methicillin 61-72-3, Cloxacillin 64-75-5, Tetracycline hydrochloride 64-77-7, Tolbutamide

64-86-8, Colchicine 65-23-6, Pyridoxine 66-79-5, Oxacillin 66-97-7, Psoralen 67-20-9, Nitrofurantoin 67-45-8, Furazolidone 67-68-5, Dimethyl sulfoxide, biological studies 68-22-4D, Norethindrone, mixt. with ethinyl estradiol 68-41-7, Cycloserine 68-88-2, Hydroxyzine 69-53-4, Ampicillin 69-72-7, biological studies 69-89-6, Xanthine 73-24-5, 6-Aminopurine, biological studies 73-31-4, Melatonin 76-42-6, Oxycodone 76-57-3, Codeine 77-09-8, Phenolphthalein 77-19-0, Dicyclomine 77-36-1, Chlorthalidone 78-44-4, Carisoprodol 80-08-0, Dapsone 81-23-2, Dehydrocholic acid 81-81-2, Warfarin 82-92-8, Cyclizine 82-95-1, Buclizine 83-43-2, Methylprednisolone 83-73-8, Iodoquinol 83-89-6, Quinacrine 83-98-7, Orphenadrine 86-54-4, Hydralazine 89-57-6, Mesalamine 90-34-6, Primaquine 90-82-4, Pseudoephedrine 91-64-5, Coumarin 92-13-7, Pilocarpine 92-84-2, Phenothiazine 93-14-1, Guaifenesin 94-20-2, Chlorpropamide 94-36-0, Benzoyl peroxide, biological studies 94-78-0, Phenazopyridine 95-25-0, Chlorzoxazone 96-64-0, Soman 97-77-8, Disulfiram 99-66-1, Valproic acid 100-33-4, Pentamidine 100-97-0, Methenamine, biological studies 101-31-5, Hyoscyamine 103-90-2, Acetaminophen 113-18-8, Ethchlorvynol 113-42-8, Methylergonovine 113-45-1, Methylphenidate 114-07-8, Erythromycin 114-86-3, Phenformin 118-42-3, Hydroxychloroquine 122-09-8, Phentermine 123-56-8, Succinimide 123-63-7, Paraldehyde 124-94-7, Triamcinolone 125-29-1, Hydrocodone 125-33-7, Primidone 125-64-4, Methyprylon 125-71-3, Dextromethorphan 125-84-8, Aminoglutethimide 126-07-8, Griseofulvin 126-52-3, Ethinamate 127-07-1, Hydroxyurea 127-69-5, Sulfisoxazole 128-13-2, Ursodiol 130-95-0, Quinine 132-17-2, Benztropine 133-10-8, Sodium p-aminosalicylate 137-58-6, Lidocaine 138-56-7, Trimethobenzamide 144-11-6, Trihexyphenidyl 147-52-4, Nafcillin 147-94-4, AraC 148-82-3, Melphalan 154-21-2, Lincomycin 154-42-7, Thioguanine 154-93-8, Carmustine 155-97-5, Pyridostigmine 298-46-4, 5H-Dibenz[b,f]azepine-5-carboxamide 298-50-0, Propantheline 299-42-3, Ephedrine 300-62-9D, Amphetamine, mixed 300-62-9D, Amphetamine, mixed salts 302-17-0, Chloral **hydrate** 302-79-4, Tretinoin 303-53-7, Cyclobenzaprine 305-03-3, Chlorambucil 315-30-0, Allopurinol 321-64-2, Tacrine 346-18-9, Polythiazide 361-37-5, Methysergide 363-24-6, Dinoprostone 364-62-5, Metoclopramide 378-44-9, Betamethasone 389-08-2, Nalidixic acid 395-28-8, Isoxsuprine 439-14-5, Diazepam 443-48-1, Metronidazole 446-86-6, Azathioprine 456-59-7, Cyclandelate 461-72-3, Hydantoin 463-04-7, Amyl nitrite 469-62-5, Propoxyphene 474-25-9, Chenodiol 480-30-8, Dichloralphenazone 484-23-1, Dihydralazine 503-01-5, Isometheptene 512-15-2, Cyclopentolate 520-85-4, Medroxyprogesterone 525-66-6, Propranolol 526-36-3, Xylometazoline 536-33-4, Ethionamide 541-15-1, Levocarnitine 546-88-3, Acetohydroxamic acid 555-30-6, Methyl dopa 564-25-0, Doxycycline 569-65-3, Meclizine 577-11-7, Docusate sodium 596-51-0, Glycopyrrolate 599-79-1, Sulfasalazine 603-50-9, Bisacodyl 634-03-7, Phendimetrazine 637-07-0, Clofibrate 657-24-9, Metformin 671-16-9, Procarbazine 672-87-7, Metyrosine 674-38-4, Bethanechol 723-46-6, Sulfamethoxazole 738-70-5, Trimethoprim 745-65-3, Alprostadil 791-35-5, Chlophedianol 797-63-7, Levonorgestrel 797-64-8D, L-Norgestrel, ethinyl estradiol mixt. 846-49-1, Lorazepam 846-50-4, Temazepam 911-45-5, Clomiphene 915-30-0, Diphenoxylate 962-58-3, Diazoxon 968-93-4, Testolactone 972-02-1, Diphenidol 990-73-8, Fentanyl citrate 1134-47-0, Baclofen 1143-38-0, Anthralin 1321-13-7, Potassium aminobenzoate 1397-89-3, Amphotericin B 1400-61-9, Nystatin 1404-04-2, Neomycin 1404-04-2D, Neomycin, mixt. with polymx/HC 1404-90-6, Vancomycin 1406-05-9, Penicillin 1491-59-4, Oxymetazoline 1622-61-3, Clonazepam 1953-02-2, Tiopronin 1977-10-2, Loxapine 2152-34-3, Pemoline 2152-44-5, Betamethasone valerate 2447-57-6, Sulfadoxine 2451-01-6, Terpin **hydrate** 2609-46-3, Amiloride 2809-21-4 2998-57-4, Estramustine 3116-76-5, Dicloxacillin 3313-26-6, Thiothixene 3385-03-3, Flunisolide 3485-14-1, Cyclacillin 3737-09-5, Disopyramide 3778-73-2, Iphosphamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

IT 3930-20-9, Sotalol 4205-90-7, Clonidine 4419-39-0, Beclomethasone 4499-40-5, Oxtriphylline, biological studies 4618-18-2, Lactulose 4697-36-3, Carbenicillin 4759-48-2, Isotretinoin 5051-62-7, Guanabenz 5543-57-7, (s)-Warfarin 5633-20-5, Oxybutynin 5786-21-0, Clozapine 6190-39-2, Dihydroergotamine mesylate 6493-05-6, Pentoxifylline 6621-47-2, Perhexiline 7020-55-5, Clidinium 7235-40-7, Beta carotene 7261-97-4, Dantrolene 7416-34-4, Molindone 7439-93-2, Lithium, biological studies 7447-40-7, Potassium chloride, biological studies 7481-89-2, Zalcitabine 7487-88-9, Magnesium sulfate, biological studies 7648-98-8, Ambenonium 7681-11-0, Potassium iodide, biological studies 7681-93-8, Natamycin 7683-59-2, Isoproterenol 8029-99-0, Paregoric

8049-47-6, Pancreatin 8050-81-5, Simethicone 8063-07-8, Kanamycin
8067-24-1, Ergoloid mesylates 9001-27-8, BLood-coagulation factor VIII
9001-75-6, Pepsin 9004-10-8, Insulin, biological studies 9004-67-5,
Methyl cellulose 9005-49-6, Enoxaparin, biological studies 9007-92-5,
Glucagon, biological studies 9039-53-6, Urokinase 9046-56-4, Ancrod
10118-90-8, Minocycline 10238-21-8, Glyburide 10262-69-8, Maprotiline
10540-29-1, Tamoxifen 11041-12-6, Cholestyramine 11056-06-7, Bleomycin
11111-12-9, Cephalosporin 12174-11-7, Attapulgite 12244-57-4, Gold
sodium thiomalate 12650-69-0, Mupirocin 12794-10-4D, Benzodiazepine,
derivs. 13010-47-4, Lomustine 13292-46-1, Rifampin 13311-84-7,
Flutamide 13392-28-4, Rimantadine 13647-35-3, Trilostane 14028-44-5,
Amoxapine 14124-50-6 14611-51-9, Selegiline 14769-73-4, Levamisole
14838-15-4, Phenylpropanolamine 14882-18-9, Bismuth subsalicylate
15301-69-6, Flavoxate 15307-86-5, Diclofenac 15663-27-1, Cisplatin
15686-71-2, Cephalexin 15687-27-1, Ibuprofen 15722-48-2, Olsalazine
16051-77-7, Isosorbide mononitrate 16068-46-5, Potassium phosphate
16110-51-3, Cromolyn 16590-41-3, Naltrexone 16679-58-6, Desmopressin
17230-88-5, Danazol 17784-12-2, Sulfacytine 18323-44-9, Clindamycin
18559-94-9, Albuterol 18883-66-4, Streptozocin 19216-56-9, Prazosin
19794-93-5, Trazodone 20537-88-6, Amifostine 20830-75-5, Digoxin
20830-81-3, Daunomycin 21256-18-8, Oxaprozin 21829-25-4, Nifedipine
22204-53-1, Naproxen 22232-71-9, Mazindol 23031-32-5, Terbutaline
sulfate 23214-92-8, Doxorubicin 23288-49-5, Probucol 25322-68-3,
Polyethylene glycol 25451-15-4, Felbamate 25614-03-3, Bromocriptine
25812-30-0, Gemfibrozil 26652-09-5, Ritodrine 26787-78-0, Amoxicillin
26807-65-8, Indapamide 26839-75-8, Timolol 27203-92-5, Tramadol
27262-47-1, Levobupivacaine 27686-84-6, Masoprocol 28395-03-1,
Bumetanide 28657-80-9, Cinoxacin 28782-42-5, Difenoxin 28860-95-9,
Carbidopa 28911-01-5, Triazolam 28981-97-7, Alprazolam 29094-61-9,
Glipizide 29110-47-2, Guanfacine 29122-68-7, Atenolol 30516-87-1,
Zidovudine 31441-78-8, Mercaptopurine 31677-93-7, Bupropion
hydrochloride 31828-71-4, Mexiletine 31883-05-3, Moricizine
32986-56-4, Tobramycin 33069-62-4, Paclitaxel 33419-42-0, Etoposide
34089-81-1, Sodium ferric gluconate 35189-28-7, Norgestimate
36322-90-4, Piroxicam 36505-84-7, Buspirone 36791-04-5, Ribavirin
38304-91-5, Minoxidil 40180-04-9, Tienilic acid 40580-59-4, Guanadrel
41575-94-4, Carboplatin 41708-72-9, Tocainide 42399-41-7, Diltiazem
42924-53-8, Nabumetone 49562-28-9, Fenofibrate 50679-08-8, Terfenadine
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51110-01-1, Somatostatin 51333-22-3, Budesonide 51384-51-1, Metoprolol
51481-61-9, Cimetidine 53179-11-6, Loperamide 53230-10-7, Mefloquine
53608-75-6, Pancrelipase 53714-56-0, Leuprolide 53994-73-3, Cefaclor
54024-22-5, Desogestrel 54063-53-5, Propafenone 54143-56-5, Flecainide
acetate 54182-58-0, Sucralfate 54350-48-0, Etretinate 54573-75-0,
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55268-75-2, Cefuroxime 55985-32-5, Nicardipine 56420-45-2, Epirubicin
58001-44-8 58581-89-8, Azelastine 59122-46-2, Misoprostol
59277-89-3, Acyclovir 59729-33-8, Citalopram 59865-13-3, Cyclosporine
A 60142-96-3, Gabapentin 60205-81-4, Ipratropium 61489-71-2,
Menotropin 61718-82-9, Fluvoxamine maleate 61869-08-7, Paroxetine
62571-86-2, Captopril 63585-09-1, Foscarnet sodium 63590-64-7,
Terazosin 64952-97-2, Latamoxef 65141-46-0, Nicorandil 65277-42-1,
Ketoconazole 66085-59-4, Nimodipine 66104-22-1, Pergolide
66357-35-5, Ranitidine 66376-36-1, Alendronate 67227-57-0, Fenoldopam
mesylate 68475-42-3, Anagrelide 68844-77-9, Astemizole 69049-73-6,
Nedocromil 69123-98-4, Fialuridine 69655-05-6, Didanosine
70359-46-5, Brominide tartrate 70989-04-7, S-Mephenytoin 71320-77-9,
Moclobemide 72432-03-2, Miglitol 72509-76-3, Felodipine 72956-09-3,
Carvedilol 73590-58-6, Omeprazole 74103-06-3, Ketorolac 74191-85-8,
Doxazosin 75330-75-5, Lovastatin 75695-93-1, Isradipine 75706-12-6,
Leflunomide 75847-73-3, Enalapril 76470-66-1, Loracarbef 76547-98-3,
Lisinopril 76568-02-0, Flosequinan 76584-70-8 76824-35-6, Famotidine
76932-56-4, Nafarelin 76963-41-2, Nizatidine 78110-38-0, Aztreonam
78628-80-5, Terbinafine hydrochloride 79516-68-0, Levocabastine
79617-96-2, Sertraline 79794-75-5, Loratadine 79902-63-9, Simvastatin
80125-14-0, Remoxipride 80474-14-2, Fluticasone propionate 81093-37-0,
Pravastatin 81098-60-4, Cisapride 81103-11-9, Clarithromycin
81669-57-0, Anistreplase 82410-32-0, Ganciclovir 82419-36-1, Ofloxacin
82626-48-0, Zolpidem 82834-16-0, Perindopril 83366-66-9,
Nefazodone 83799-24-0, Fexofenadine 83881-51-0, Cetirizine
83905-01-5, Azithromycin 84057-84-1, Lamotrigine 84449-90-1,
Raloxifene 84625-61-6, Itraconazole 85441-61-8, Quinapril
85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 86541-75-5,
Benazepril 87333-19-5, Ramipril 87679-37-6, Trandolapril 88040-23-7,
Cefepime 88150-42-9, Amlodipine 89365-50-4, Salmeterol 89778-26-7,
Toremifene 90566-53-3, Fluticasone 91714-94-2, Bromfenac 92665-29-7,
Cefprozil 93390-81-9, Fosphenytoin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); BIOL (Biological study)
(methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

L3 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 2000:875749 CAPLUS
DN 134:33001
TI Alkali metal and alkaline-earth metal salts of acetaminophen
IN Ohannesian, Lena A.; Nadig, David; Higgins, John D., III; Rey, Max; Martellucci, Stephen A.
PA McNeill-PPC, Inc., USA
SO U.S., 10 pp., Cont.-in-part of U.S. Ser. No. 987,210, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6160020	A	20001212	US 1998-100284	19980619
	WO 9966919	A1	19991229	WO 1999-US13064	19990609
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9943380	A1	20000110	AU 1999-43380	19990609
PRAI	US 1996-771176	B2	19961220		
	US 1997-987210	B2	19971209		
	US 1998-100284	A	19980619		
	WO 1999-US13064	W	19990609		

AB Isolated salts of acetaminophen are disclosed. Alkali metal and alk.-earth metal salts of acetaminophen are formed by reacting the free acid of acetaminophen with the corresponding metal hydroxide and then immediately isolating the resulting salt. These salts have been found to be more water sol. and less bitter in taste than the free acid form of acetaminophen. The isolated salts may also be combined with other active ingredients. A tablet contained calcium acetaminophen 368.23, chlorpheniramine maleate 2, microcryst. cellulose 520.77, silica 4.5, and Mg stearate 4.5 mg.

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 50-78-2, Acetyl salicylic acid 51-43-4, Epinephrine 51-55-8, Atropine, biological studies 53-86-1, Indomethacin 58-08-2, Caffeine, biological studies 58-55-9, Theophylline, biological studies 58-73-1, Diphenhydramine 59-33-6, Pyrilamine 59-42-7, Phenylephrine 60-87-7, Promethazine 68-88-2, Hydroxyzine 73-31-4, Melatonin 76-42-6, Oxycodone 76-57-3, Codeine 77-09-8, Phenolphthalein 77-19-0, Dicyclomine 77-22-5, Caramiphen 77-23-6, Carbetapentane 86-22-6, Brompheniramine 90-82-4, Pseudoephedrine 91-81-6, Tripelennamine 93-14-1, Guaifenesin 104-31-4, Benzonatate; 113-92-8 125-29-1, Hydrocodone 125-71-3, Dextromethorphan 128-62-1, Noscapine 129-03-3, Cyproheptadine 132-21-8, Dexbrompheniramine 299-42-3, Ephedrine; 317-34-0, Aminophylline 364-62-5, Metoclopramide 466-99-9, Hydromorphone 471-34-1, Calcium carbonate, biological studies 486-12-4, Triprolidine 554-10-9, 3-Iodo-1,2-propanediol 562-10-7, Doxylamine 586-06-1, Metaproterenol 606-04-2, Pamabrom. 616-91-1 642-72-8, Benzydamine 791-35-5, Chlophedianol 915-30-0, Diphenoxylate 2451-01-6, Terpin **hydrate** 3572-43-8, Bromhexine 3964-81-6, Azatadine 5104-49-4, Flurbiprofen 7020-55-5, Clidinium 7683-59-2, Isoprenaline 8050-81-5, Simethicone 12125-02-9, Ammonium chloride, biological studies 14838-15-4, Phenylpropanolamine 14882-18-9, Bismuth subsalicylate 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 16958-94-4 18053-31-1, Fominoben 18559-94-9, Albuterol; 18683-91-5, Ambroxol 21645-51-2, Aluminum hydroxide, biological studies 22071-15-4, Ketoprofen 22204-53-1, Naproxen 23031-25-6, Terbutaline 25523-97-1, Dexchlorpheniramine 27203-92-5, Tramadol 29679-58-1, Fenoprofen 29975-16-4, Estazolam 30392-40-6, Bitolterol 33005-95-7, Tiaprofenic acid 34580-13-7, Ketotifen 35719-43-8 36322-90-4, Piroxicam 36950-96-6, Cicloprofen 38194-50-2, Sulindac 41340-25-4, Etodolac 42924-53-8, Nabumetone 50679-08-8, Terfenadine 51481-61-9, Cimetidine 51803-78-2, Nimesulide 53179-11-6, Loperamide; 53716-49-7, Carprofen 54182-58-0, Sucralfate 57644-54-9, Bismuth subcitrate 61869-07-6, Domiodol 66357-35-5, Ranitidine 68844-77-9, Astemizole 71125-38-7, Meloxicam 73590-58-6, Omeprazole 74103-06-3, Ketorolac 74978-16-8, Magaldrate 75970-99-9, Norastemizole

76824-35-6, Famotidine 76963-41-2, Nizatidine 79794-75-5, Loratidine 80937-31-1, Flosulide 81098-60-4, Cisapride **82626-48-0**, Zolpidem 83799-24-0, Fexofenadine; 83881-51-0, Cetirizine 86181-42-2, Temelastine 87848-99-5, Acrivastine 169590-42-5, Celecoxib 180200-68-4 209967-48-6 209967-50-0 209967-51-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral compns. contg. acetaminophen metal salt and other actives)

L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 1999:819235 CAPLUS
DN 132:54898
TI Pharmaceutical composition containing a salt of acetaminophen and at least one other active ingredient
IN Ohannesian, Lena A.; Nadig, David; Higgins, John D., III; Rey, Max; Martellucci, Stephen A.
PA Mcneil-PPC, Inc., USA
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9966919	A1	19991229	WO 1999-US13064	19990609
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6160020	A	20001212	US 1998-100284	19980619
AU 9943380	A1	20000110	AU 1999-43380	19990609
PRAI US 1998-100284	A	19980619		
US 1996-771176	B2	19961220		
US 1997-987210	B2	19971209		
WO 1999-US13064	W	19990609		

AB This invention relates to pharmaceutical compns. comprising an alkali or alk.-earth metal salt of acetaminophen and at least one other active ingredient selected from the group consisting of analgesics, decongestants, expectorants, antitussives, antihistamines, gastrointestinal agents, diuretics, bronchodilators and mixts. thereof. The acetaminophen salts have both improved aq. soly. and a less bitter taste than the free acid form of acetaminophen. A tablet contained acetaminophen calcium salt 368.23, chlorpheniramine maleate 2, microcryst. cellulose 520.77, Cab-O-Sil M5 4.5, and Mg stearate 4.5 mg.
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT 50-78-2, Acetylsalicylic acid 51-43-4, Epinephrine 51-55-8, Atropine, biological studies 53-86-1, Indomethacin 58-08-2, Caffeine, biological studies 58-55-9, Theophylline, biological studies 58-73-1, Diphenhydramine 59-33-6, Pyrilamine 59-42-7, Phenylephrine 60-87-7, Promethazine 68-88-2, Hydroxyzine 73-31-4 76-42-6, Oxycodone 76-57-3, Codeine 77-09-8, Phenolphthalein 77-19-0, Dicyclomine 77-22-5, Caramiphen 77-23-6, Carbetapentane 86-22-6, Brompheniramine 90-82-4, Pseudoephedrine 91-81-6, Tripelennamine 93-14-1, Guaifenesin 103-90-2 104-31-4, Benzonatate 113-92-8, Chlorpheniramine maleate 125-29-1, Hydrocodone 125-69-9, Dextromethorphan hydrobromide 125-71-3, Dextromethorphan 128-62-1, Noscapine 129-03-3, Cyproheptadine 132-21-8, Dexbrompheniramine 147-24-0, Diphenhydramine hydrochloride 299-42-3, Ephedrine 317-34-0, Aminophylline 345-78-8, Pseudoephedrine hydrochloride 364-62-5, Metoclopramide 466-99-9, Hydromorphone 471-34-1, Calcium carbonate, biological studies 486-12-4, Triprolidine 554-10-9, 3-Iodo-1,2-propanediol 562-10-7, Doxylamine 586-06-1, Metaproterenol 606-04-2, Pamabrom 616-91-1, N-Acetylcysteine 642-72-8, Benzydamine 791-35-5, Chlophedianol 915-30-0, Diphenoxylate 2451-01-6, Terpin **hydrate** 3572-43-8, Bromhexine 3964-81-6, Azatadine 5104-49-4, Flurbiprofen 7020-55-5, Clidinium 7683-59-2, Isoprenaline 8024-48-4, Casanthranol 8050-81-5, Simethicone 12125-02-9, Ammonium chloride, biological studies 14838-15-4, Phenylpropanolamine 14882-18-9, Bismuth subsalicylate 15307-86-5, Diclofenac 15687-27-1 16958-94-4 18053-31-1, Fominoben 18559-94-9, Albuterol 18683-91-5, Ambroxol 21645-51-2, Aluminum hydroxide (Al(OH)3), biological studies 22071-15-4, Ketoprofen 22204-53-1, Naproxen 23031-25-6, Terbutaline 25523-97-1,

Dexchlorpheniramine 27203-92-5, Tramadol 29679-58-1, Fenoprofen 29975-16-4, Estazolam 30392-40-6, Bitolterol 33005-95-7, Tiaprofenic acid 34580-13-7, Ketotifen 35719-43-8 36322-90-4, Piroxicam 36950-96-6, Cicloprofen 38194-50-2, Sulindac 41340-25-4, Etodolac 42924-53-8, Nabumetone 50679-08-8, Terfenadine 51481-61-9, Cimetidine 51803-78-2 53179-11-6, Loperamide 53716-49-7, Carprofen 57644-54-9, Bismuth subcitrate 61869-07-6, Domiodol 66357-35-5, Ranitidine 68844-77-9, Astemizole 71125-38-7, Meloxicam 73590-58-6, Omeprazole 74103-06-3, Ketorolac 74978-16-8, Magaldrate 75970-99-9, Norastemizole 76824-35-6, Famotidine 76963-41-2, Nizatidine 79794-75-5, Loratidine 80937-31-1, Flosulide **82626-48-0**, Zolpidem 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 86181-42-2, Temelastine 87848-99-5, Acrivastine 169590-42-5, Celecoxib 180200-68-4 209967-47-5 209967-48-6 209967-50-0 209967-51-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. contg. acetaminophen salts and other drugs)